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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/728,207	12/01/2000	Yoshiyuki Nagai	50026/005002	4421

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EXAMINER	
MOSHER, MARY	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/18/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/728,207	Nagai et al
Examiner	**Art Unit**
Mosher	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *7/24/2002, 8/12/2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *09/071,591* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *14, 15*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Double Patenting

Claims 1-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 11-12, 14 of copending Application No. 09/132,521, for reasons of record.

Claims 11 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7-11 of copending Application No. 09/436,504, for reasons of record. **This is not an erroneous serial number. This application has an inventor in common with the instant application.**

Claims 1-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 09/702,498, for reasons of record.

Claims 1-5 and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 09/823,699, for reasons of record.

Applicants indicate that the amendments render the rejections moot; however, as discussed below, the response further confuses the intended scope of the invention, so the examiner is unable to determine whether or not the amended claims are distinct from claims in the copending applications. Applicants offer to submit a terminal disclaimer once the claims of the

pending application are patented; however, since no disclaimer has ben filed, the rejections must be maintained.

Claim Rejections - 35 USC § 112, 2nd

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claim fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in Paper No.12 filed 7/24/2002. This rejection involves the recitation "disseminative capability" in the claims. In the response filed 7/24/2002, applicants indicate that, contrary to the assumption made in the last Office action, "disseminative" is not equivalent to "non-defective", but "disseminative capability" is defined in the specification as "the capability to form infectious particles or their equivalent complexes and disseminate them to other cells following the transfer of nucleic acid into host cells by infection or artificial techniques and the intracellular replication of said nucleic acid." This definition is circular, it defines disseminative capability as the ability to disseminate, and now it is very unclear what applicant means by "disseminate". Webster's dictionary defines "disseminate" as "to scatter far and wide; spread abroad, as if sowing; promulgate widely." This ordinary definition does not help to understand what applicants mean. The examiner thinks that the specification sentence probably means that nucleic acids are transferred to host cells by infection or artificial techniques, the nucleic acid replicates, and infectious particles (or their

equivalents, whatever that means) are formed and get themselves into other cells[1]. Applicant states that the claimed vector can be defective in the areas of replication and infection so long as it retains the ability to disseminate. But if the vector is defective in replication, it cannot fulfill the specifications's requirement regarding "intracellular replication of said nucleic acid." If the vector is defective in infection, how can it "disseminate?" After reading applicant's response, the examiner no longer has any clue as to the intended meaning of "disseminative capability", or any clue regarding the intended scope of applicant's claims (except insofar as they require insertion of a foreign gene or deletion or alteration of a Sendai gene).

Furthermore, in the arguments directed to the Conzelmann reference, applicants argue that "the 'mutations' contemplated by the present invention comprise deletions or inactivation of the Sendai virus *replication factors* NP, P, and L, but not deletions or inactivations of the Sendai dissemination genes *dissemination factors*, M, F, and HN." Can applicant point to any discussion communicating this concept in the specification? Support for this concept was not apparent to the Examiner in reading the specification as a whole.

For these reasons, the statements made in applicant's response indicate that the invention is different from what is defined in the claim(s), because the response indicates that the intention involves limitations that do not appear to be reasonably communicated by the specification supporting the claims.

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[1]or does "following the transfer or nucleic acids into host cells by infection or artificial techniques" also refer to a mechanism for "dissemination"??

Please note, the examiner does understand reconstitution of infectious viruses from nucleic acids (see for example US patents 5,578,473; 5,217,879; 5,445,953; 5,665,362; 5,780,280; 6,231,868, all issued by this examiner). The examiner further understands that reconstituted infectious virus can include a variety of packaged genomes such as wild-type genomes, mutated genomes, genomes lacking genes required for replication, genomes lacking genes required for packaging, and gutless genomes lacking everything but cis-acting packaging sequences. What the examiner does not understand is the scope that applicants intend to claim in this application.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Since it is now unclear what is meant by "disseminative capability", it is not clear what "the disseminative capability of wild-type Sendai virus" means. A reasonable interpretation of "the disseminative capability of wild-type Sendai virus" would be that the virus has the same propagation characteristics as a wild-type virus; however, this interpretation is challenged by the requirement in claim 2 that genes encoding functional proteins be altered, and by applicant's argument that the claimed virus can be defective.

In addition, in claim 1, "Sendai virus" has been changed to "Sendai viral vector", and "desired gene deleted or inactivated" has been changed to "Sendai viral gene deleted or altered." It appears that the intent is to claim a product which either has a foreign gene inserted in a Sendai virus genome, or a deletion or alteration of a Sendai gene. In regard to the "gene altered" embodiment, if the intent is a modified Sendai product without a foreign gene, how is "a

recombinant Sendai viral vector" distinguished from an ordinary Sendai virus modified by a different method (e.g., any virus variant isolated by classical methods)? Does the "disseminative capability of wild-type" element mean that any product which "disseminates" differently from a wild type virus is excluded? Is the intent really to exclude phenotypic differences from the wild-type "dissemination" such as host range alterations, differences in plaque size or burst size, temperature-sensitivity, changes in tissue trophism or virulence? These questions are asked because the answers to questions such as these determine the metes and bounds of the claimed subject matter.

Claim 13, part b, lacks antecedent for "the reconstituted".

Claims 18-19 are drawn to vector or virus "produced entirely without the use of a helper virus." It is not clear if there are any measurably different characteristics between vectors and viruses produced with or without a helper virus, so it is not clear what the difference is between claims 18-19 and parent claims 1 & 14. Is the intent of claims 18-19 to be product-by-process claims?

Claims 20-25 require the host to "not express heterologous RNA polymerase." However, the parent claims 7-10 require the host cell to express "Sendai viral proteins NP, P, and L", and it is not clear how one can express the proteins of the Sendai RNA polymerase complex without expressing an RNA polymerase heterologous to the host cell. Similarly, parent claims 11-12 involve expression of a protein from a cell infected with a disseminative Sendai viral vector, and it is not clear how the viral vector can operate without expressing its polymerase activity.

Claim 26 lacks antecedent for "said host" in claim 14.

Claim Rejections - 35 USC § 112, 1st

Claims 14-17, 19, and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "new matter" rejection. Applicant is requested to point to support in the specification as filed for the limitations in claim 14, parts (b) and (c), as the examiner is unable to find support for the intergenic and downstream insertion sites recited in the claim. This affects the dependent claims. In addition, applicant is requested to point to support for a disseminative virus with NP, P, or L deleted, as recited in claim 15.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Sendai virus with a foreign gene insertion before the NP ORF, does not reasonably provide enablement for the full scope of "disseminative" viruses. As extensively discussed above, it is not at all clear what applicant means by a "disseminative" virus. If one cannot understand what is claimed, one cannot make or use what is claimed. The specification teaches how to make a Sendai virus with a foreign gene inserted before the NP ORF, so this is enabled. The specification does not teach any other sites in which one could insert foreign sequences, does not teach deletions or alterations which result in a self-propagating virus, and does not teach trans-complementation of defective Sendai genomes with defects in replication or packaging genes. Considering the vague and indefinite scope of the claims and the limited

teachings in the specification, it is concluded that undue experimentation would be required to make the full scope of whatever is claimed.

Priority

Applicant has filed certified translations of the priority documents, PCT/JP96/03069 and JP Hei 7-285417. After carefully analyzing the translations, applicant is denied the benefit of their filing dates for the following reasons.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In order to be granted the benefit of the filing date of a priority application, said application must meet the requirements of 35 USC 112, first paragraph.

In the case of the JP application, the application does not contain an adequate written description of the invention now claimed. The application, in general terms, conveys a desire to obtain disseminative Sendai viruses with gene modifications or foreign gene insertions, and even identifies some of the genes which would be desirable to alter, but the application does not discuss the viruses in sufficient detail to reasonably convey to those skilled in the art that applicants actually possessed any of the desired modified viruses. The application does not disclose any specific characteristics of modified viruses, such as where in the structure of any of the virus genes one can make alterations without affecting disseminative capability, or where in the virus genome one can insert a foreign gene without affecting disseminative capability. One skilled in the

art cannot a priori predict where any such alterations can be made without creating a defective virus. Therefore it is concluded that the JP application does not meet the written description requirement of 35 USC 112, first paragraph.

In the case of the PCT application, additional disclosure includes a discussion of two working examples of Sendai virus modified by insertion of foreign genes (Examples 5-7). It is clear from these working examples that applicants reduced to practice the "foreign gene" embodiment of the claimed invention. However, the PCT application does not disclose where in the genome these foreign genes were inserted. The disclosure in the PCT application is limited to statements that the foreign sequences were 'inserted into the NotI site of "pSeV18+".' However, the PCT application never discloses anything about the structure of "pSeV18+", or where the NotI site is. Therefore, although the PCT application reasonably conveys that applicants possessed at least part of the invention claimed, the PCT application does not enable the working examples which convey possession, and apparently conceals the best mode of operation of the invention. The conclusion that the best mode is concealed in necessitated by the failure of the PCT application to disclose a key piece of information (the insertion site) that is essential to understand and reproduce the working examples.

For these reasons, it is maintained that the effective filing date for the invention claimed is December 01, 2000.

Claim Rejections - 35 USC § 102

Claims 1-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al (Genes to Cells 1:569-579, 1996). See pages 573-574. Applicants argue that this reference is not available as prior art; however, as discussed above, applicant is denied benefit of the earlier-filed applications.

Claims 1-14, 16, 17-19, 25, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hassan et al or Sakai et al or Toriyoshi et al (all cited in IDS) . Although the publications do not teach a process which is entirely without use of a helper virus or a first host cell which does not express a heterologous polymerase, the product of these processes is indistinguishable from the vaccinia-free virus produced by a different method, and the allantoic fluid containing the vaccinia-free virus. Therefore, the references anticipate product-by-process claims 18, 25, and 26.

Claim Rejections - 35 USC § 103

On reconsideration, the rejection of claims 1-13 under 35 U.S.C. 103(a) as being unpatentable over Conzelmann 6,033,886 is withdrawn. Since Conzelmann teaches use of a vaccinia virus as part of the virus reconstitution method, and since Sendai virus virion assembly is prevented by vaccinia virus, it is concluded that Conzelmann does not teach a method which is enabling for Sendai virus.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 7/24/2002 prompted some new ground(s) of rejection presented in this Office action. Applicant's amendment necessitated the other new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

October 17, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800 1600